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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/436,892	MEDFORD ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,15,21-27,30-32,35,36,40 and 41* is/are pending in the application.

4a) Of the above claim(s) *7-9,11-14,16-20,29 and 37-39* is/are withdrawn from consideration.

5)☒ Claim(s) *15,31,32,35 and 36* is/are allowed.

6)☒ Claim(s) *1-6, 10, 21-27, 30, 40, and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-6,10,15,21-27,30-32,35,36,40 and 41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 6/2/03 in Paper No. 18 is acknowledged and has been entered. Claims 1, 6, 9, and 15 have been amended. Claims 28, 33, and 34 have been cancelled. Claims 37-41 have been added. Claims 1-27, 29-32, and 35-41 are pending.

Newly submitted claims 37-39 and amended claims 9 and 29 are directed to new inventions that are independent or distinct from the inventions originally claimed for the following reasons: 1) claims 37-39 are drawn to assessing uptake of cholesterol-containing low density lipoprotein into cell culture, and 2) claims 9 and 29 are now drawn to method of determining whether a compound binds and increases the clearance of a low density lipoprotein using three distinct antibodies.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 7-9, 11-14, 16-20, 29, and 37-39 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 1-6, 10, 15, 21-27, 30-32, 35, 36, and 40-41 are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 102

2. The rejection of claims 28, 33, and 34 are now moot in light of Applicant's cancellation of the claims.

3. In light of Applicant's amendment and arguments, the rejection of claims 1-5, 15, 21-22, 31-32, and 35-36 under 35 U.S.C. 112, second paragraph, is hereby withdrawn.

4. In light of Applicant's arguments, the rejection of claims 1-6, 9-10, 15, and 21-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parthasarathy (US 5,262,439) in view of Koren et al. (US 6,107,045) is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 6, 10, 23-27, 30, 40, and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6, step iii) has improper antecedent basis problem in reciting, "a lipoprotein receptor". Perhaps, Applicant intends "the LDL receptor" for consistency and proper antecedent basis in claim language.

Claim 30 lacks clear antecedent support in reciting, "the CC-LDL". Specifically, there is no requirement in this set of claims that the LDL is "cholesterol containing LDL".

Claim 40, step iii) is vague and indefinite because it is unclear how the second antibody, having a label attached thereto, detects the combination in step ii), i.e. binds an element within the combination in step ii).

Claim 40, step v) is indefinite and lacks antecedent basis in reciting, "captured by the assay"

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The claims are drawn to a method wherein a compound is administered to a human host to enhance clearing of cholesterol-containing low density lipoproteins, from here on CC-LDL. The CC-LDL is isolated from the host and is determined for a change in the three dimensional conformation of the lipoprotein, wherein a change in the three dimensional conformation of the lipoprotein is detected by antibody binding to a specific epitope of the lipoprotein, i.e. apoB-100, which subsequently binds the LDL receptor.

The claimed invention purports this mechanism to enhancing the clearance of LDL. At page 14 of the specification, the compounds are identified as monosuccinic acid esters of probucol. Accordingly,

6. Claims 1-3, 6, 21-24, 27, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Somers (US 6,121,319).

Somers teaches that compounds consisting of monoesters of probucol are effective in simultaneously reducing cholesterol and lowering LDL; thus are composite cardiovascular agents. Specifically, Somers teaches that monosuccinic acid esters of probucol reduces HDL to a small extent in rabbits, while probucol reduces LDL to a small extent and reduces HDL significantly. Somers also teaches that monosuccinic esters of probucol block the induced expression of endothelial cell surface adhesion molecule, VCAM-1; thus, are useful in the treatment of atherosclerosis and other cardiovascular disease (See Summary at columns 5 and 6). In Examples 5 and 8, Somers exemplifies the effect of monosuccinic esters of probucol on cholesterol in plasma of lipid-fed animals by 1) administering monosuccinic esters of probucol to rabbits fed with high fat and high cholesterol diet and 2) observing for effects on total cholesterol and cholesterol containing lipoproteins, i.e. LDL, VLDL, and HDL (CC-LDL) by obtaining and separating lipoprotein fractions from rabbit plasma by fast phase chromatography then analyzing for cholesterol and lipoprotein content. Somers found that the monosuccinic acid esters of probucol resulted in statistically significant reduction in total cholesterol and CC-LDL. According to Somers, chylomicrons, VLDL, and LDL participate in the transport of cholesterol between other peripheral tissues, i.e.

intestinal and adipose, and liver (hepatic LDL receptors). Specifically, VLDL and LDL transports cholesterol from liver to other peripheral tissues, i.e. LDL receptors.

Somers is silent in teaching that binding occurs between the compound (consisting of monosuccinic esters of probucol) and CC-LDL; thus resulting to a change in binding affinity of CC-LDL to LDL receptors.

However, the instant claims which recite "binding of the compound to LDL which enhances LDL clearance after subsequent binding to the LDL receptor", merely provide a newly discovered mechanism of a known compound which is monosuccinic acid ester of probucol, and method for use, thereof, wherein enhanced clearing of LDL subsequently results. Specifically, newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent. The claim language is only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claims.

Additionally, "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old known composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999). Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical

structure of the compound, i.e. monosuccinic esters of probucol, the properties Applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

7. Claims 4, 5, 10, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Somers (US 6,121,319) in view of Koren et al. (US 6,107,045).

Somers has been discussed supra. Somers differs from the instant invention in failing to disclose assessing CC-LDL by sandwich immunoreactive assay and/or agarose electrophoresis

Koren et al. disclose quantifying immunoreactive concentrations of lipoprotein and apolipoprotein, including apoB-100 (LDL and VLDL) using sandwich immunoreactivity assays wherein antibodies specific to apoB-100 (known to be important in LDL receptor binding process) are immobilized into microwells as capture antibodies and labeled as secondary antibodies to capture and quantify the LDL concentration, respectively (see columns 11-12). Immunoreactive concentration of LDL is determined by ELISA or polyacrylamide gel electrophoresis (see columns 13, 18, and 20).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the sandwich immunoassay or agarose electrophoresis methods taught by Koren to detect reduced levels of cholesterol-containing lipoproteins in the method of Somers, which result from effective binding of the monosuccinic esters of probucol to CC-LDL because Koren specifically taught that his assay provides

antibodies specific for epitopes required for quantitation of LDL, VLDL, or apoB-100 for use in determining accurate lipid levels in serum and plasma samples.

Response to Arguments

8. Applicant's arguments have been considered but are moot in view of the new grounds of rejection.

9. Claims 15, 31, 32, 35, and 36 are allowable. Claims 40 and 41 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
September 30, 2003

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641